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(54) Title: FOAMABLE BIOCIDE COMPOSITION

(57) Abstract

A biocidal composition comprising: (a) an alcoholic chlorhexidine solution, (b) from .1 to 20% w/w of a quick breaking foaming agent, (c) from 3 to 30% w/w of an aerosol propellant and optionally (d) a corrosion inhibitor.

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FOAMABLE BIOCIDE COMPOSITION

BACKGROUND OF THE INVENTION

The present invention relates to a foamable biocidal composition.

The chemical control of bacteria and viruses is assuming increasing importance in the hospital and medical environment. Outbreaks of infections such as Methyicylin resistant Staph Aureus are causing illness, death and even temporary closure of wards in some hospitals.

This situation has been exacerbated by the failure of many bacteria to respond to conventional antibiotics. Accordingly, the need for effective control of bacterial and virus organisms is assuming greatly increased significance.

In the case of hand and skin disinfection a biocidal agent needs to kill the widest possible range of microorganisms in the least possible time without toxicity, irritation or other hazard and have a long shelf life.

Typical of these biocides are chlorine, iodophors and organic chemicals such as chlorhexidine which are commonly employed in hospitals and surgeries. The most widely accepted form of safe, effective biocide is chlorhexidine gluconate in aqueous ethanol. A full discussion of this product appears in the paper entitled "Detergents compared with each other and with antiseptics as skin 'degerminating agents'" by H.A. Lily et al in Journal of Hygiene (U.K.). Further technical disclosure of the product appears in Australian Patents Nos. 157,758 and 222,033. Conventionally, chlorhexidine is commercially supplied in a pump pack or manufactured by the hospital pharmacist as required.

Unfortunately, however, in use alcoholic chlorhexidine has inherent difficulties including the following:

(1) Openable bottles of alcoholic chlorhexidine are subject to contamination both at the time of fitting the pump head and when the pump is being operated.

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(2) The 60-70% aqueous ethanol system is highly flammable. Spillage from the plastic bottle or dispenser at any time could result in a fire.

(3) The mist as applied from pump dispensers is a highly flammable mist. This could be highly dangerous since it is being sprayed directly onto the skin.

(4) The spray mist does not confine itself to the target area, wastage occurs due to overspray.

(5) The alcoholic lotion as sprayed on the skin is difficult to control due to its low viscosity. It tends to run off the skin and evaporate rapidly before being evenly distributed.

(6) The shelf life of pump packs of a volatile fluid such as alcohol is restricted by the fact that they do not seal the pack perfectly and evaporation can occur over a period of time.

(7) The spray or lotion product is messy to use since once one hand has been sprayed it must become contaminated as the pack is held to spray the other hand.

Accordingly, it is well known that chlorhexidine must be formulated very carefully to optimise its biocidal performance.

DESCRIPTION OF THE INVENTION

With the above difficulties in mind, the present invention provides an improved composition containing alcoholic chlorhexidine in aerosol form which is easy and safe to use. In this respect, extensive research over several years was necessary on a variety of differing types compositions before the viability of an aerosol type became apparent.

Accordingly, a biocidal composition is provided comprising:

(a) an alcoholic chlorhexidine solution

(b) from .1 to 20% w/w of a quick break foaming agent

(c) from 3-30% w/w of an aerosol propellant and

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optionally

(d) a corrosion inhibitor

The inclusion of a corrosion inhibitor is necessary where the compositionn is stored in metal containers which are typical of tin plate or aluminium to counteract the corrosive nature of chlorexidine formulations. However, if the container is to non metal e.g. glass the inclusion of a corrosion inhibitor is not necessary.

As stated the composition of the invention is an aerosol form. This is most appropriate for a biocide as it avoids or minimizes the conventional defects of contamination and spillage. Pressurized aerosol containers are readily available, have been extensively tested and are well accepted.

PREFERRED FEATURES OF THE INVENTION

In an effort to minimize the aforementioned difficulty of overspray and early evaporation, a foaming agent was included, more particularly of a quick break foam variety. This has the ability of providing a thick ball of foam which disintegrates easily when spread. Proper coverage can be effected to the surface to be cleansed without premature evaporation. A general discussion of quick break foams can be found in Australian Patent 463,216. In a preferred embodiment of the present invention, a particular quick breakfoaming agent has been developed which has not been previously disclosed in this context.

This composition comprises

(a) an aliphatic alcohol preferably in amounts from 40-90% w/w composition more preferably 55-70 % w/w and most preferably 60% w/w,

(b) water preferably in amounts from 10-40 % w/w

(c) a fatty alcohol preferably in amounts from 5-10% % w/w

and

(d) a surface active agent preferably an ethoxylated

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sorbitan ester (as emulsifier); typically in amounts from .1-15% w/w.

From the viewpoint of performance it was known from the paper of H.A. Lilly et al that aqueous ethanol of approximately 70% w/w ethanol concentration is the best vehicle for chlorhexidine and this is the preferred form for use in the present composition.

It is also well known that a base formulation of chlorhexidine in aqueous ethanol tends to degrease and dry out the skin when used regularly (e.g. 40 times per shift) in the hospital environment. Thus, an emollient is optionally incorporated which would help prevent dehydration of the skin without hindering the performance of chlorhexidine. Emollients which are particularly preferred are lanolin and polyols selected from glycerol, propylene glyerol, sorbitol and low molecular weight polymers thereof. Other examples of emollients are vinyls alcohol and polyvinyl pyrollidone.

When considering the preferred requirement for 70% w/w ethanol, it was found that the composition may have an effect on the solubility characteristics of other additive e.g. fatty alcohols, lanolin and organic acid salts. It is believed the other additives react with the chlorhexidine causing it to be, to some extent, either precipitated or inactivated. Nevertheless, such compositions are still found to be useful.

The chlorhexidine component will normally be present in amounts of from .1-10% w/w though larger concentrations were found to be possible but with deleterious effects on the efficiency of entire system. Preferred forms of chlorhexidine are as a gluconate, diacetate, hydrochloride or other salts thereof.

Care should be taken to select a propellent most compatable to the entire system and in this respect the propellant is preferably selected from a group comprising propane, butane, dichloro difluoro methane, dichloro tetra fluoro ethane, octafluoro cyclo butane. As mentioned the

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propellant should be presenting amounts from 3 - 30% w/w' though preferably from about 5 to 15% w/w and more preferabely from 8 to 10% w/w.

Where the container is metal it is necessary to incorporate a corrosion inhibitor. This became apparent when researching the invention as several working formulation were achieved which however were found to corrode tin plate or aluminium containers at extraordinary rates resulting in short shelf lives. Typical corrosions inhibitors were organic acid salts more preferably sorbic acid, benzoic acid, sodium benzoate and potassium sorbate.

These inhibitors are preferably present in amounts of from .1 to 15% wt and more preferably for .1 to 3% w/w.

Thus, a typical formulation of the present invention is as follows:

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	% w/w
Propellant (e.g. propane, butane, dichloro difluoro methane, dichloro tetra fluoro ethane, octafluoro cyclo butane and mixtures thereof)	3 - 30
Chlorhexidine (as gluconate, diacetate hydrochloride and mixtures thereof, & other salts)	.1 - 10
Fatty alcohol (e.g. cetyl, stearyl, lauryl, myristyl, palmityl and mixtures thereof)	.5 - 10
Aliphatic alcohol (e.g. methyl, ethyl, isopropyl, butyl and mixtures thereof)	40 - 90
Water	10 - 40
Polyol (e.g. glycerol, propylene glycol, sorbitol & low molecular weight polymers thereof)	1 - 10
Organic acid salt (e.g. sorbic acid, benzoic acid)	.1 - 15
Surface active agent (e.g. ethyoxylated sorbitan stearate, palmitate, oleate, nonyl phenol ethoxylates, fatty alcohol ethoxylates)	.1 - 15

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	% w/w
Particularly Preferred formulations	
Chlorhexidene gluconatate 20%	5.0
Cetyl stearyl alcohol	2.5
Ethoxylated sorbitan monostearate	0.5
Propylene glycol	3.0
Ethyl alcohol (95%)	57.0
Sodium benzoate	0.2
Purified water	22.8
Dichloro difluoro methane)	
Dichloro tetrafluoro ethane) blend	9.0
	100.0
Chlorhexidine diacetate	1.0
Myristyl alcohol	3.0
Ethoxylated cetylalcohol	0.8
Clycerol	2.5
Isopropyl alcohol	60.0
Potassium sorbate	0.3
Purified water	25.4
Butane/propane	7.0
	100.0
Chlorhexidine gluconate 20%	5.0
Myristyl alcohol	3.0
Glycerol	2.5
Ethoxylated myristyl alcohol	0.8
Ethyl alcohol 95%	58.0
Postassium sorbate	1.0
Purified water	20.3
Dichloro difluoro methane)	
Dichloro tetrafluoro ethane)	10.0
	100.0

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The following are details of tests which were carried out of such formulations in which the formulation is identified by the Trade mark HEXIFOAM.

TEST A

A series of In-vitro tests were performed on "Hexifoam" to determine the efficacy of the Chlorhexidine within this formulation.

The tests were designed to establish whether any loss of biocidal activity of the chlorhexidine was occurring. Comparative evaluations were also performed utilizing "Hexifoam" (without Chlorhexidine) and unformulated non-alcohol Chlorhexidine Gluconate Standard.

The product was evaluated in a suspension test based on the principles outlined in BS.3286 under the following test conditions.

Product Dilutions:	1:2 v/v, 1:4 v/v
Contact Time;	1 minute, 2 minutes, 3 minutes 5 minutes
Organism:	Pseudomonas aeruginosa NCTC 6749
Organic Challenge:	10% Sheep Serum
Inoculum Density:	106 - 107 orgs/ml.
Product Diluent:	Distilled Water with 10% Sheep Serum
Inactivator:	Nutrient Broth N.2, Lecithin, Tween 80
Temperature:	Ambient

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Results

Test Organism: Pseudomonas aeruginosa

Sample	Dilution/ Concentration	Initial Count per ml	Surviving Organisms per ml. 1min	2min	3min	5min
Hexifoam	1:2	8.0×10^6	10	10	10	10
Hexifoam without Chlorhexidine	1:2	8.0×10^6	10	10	10	10

			1 min	2 mins	3 mins
Hexifoam	1:4[1]	3.9×10^6	10	10	10
Hexifoam without Chlorhexidine	1:4	3.9×10^6	1,500,000	800,000	500,000
Chlorhexidine Gluconate	0.25%	5.0×10^6	10	10	10

Notes

1 At 1:4 dilution of Hexifoam the concentration of Chlorhexidine is 0.25%.

2 ' / ' indicates less than
Less than 10 is the detection sensitivity of the test method i.e. no surviving organisms detected.

Conclusion

The results have indicated that a dilution of the product Hexifoam of 1:4 v/v continues to demonstrate excellent biocidal properties while the base material without chlorhexidine fails to show any significant

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biocidal properties. This is indicative of little or no loss of activity of the chlorhexidine within the formulation.

The comparative tests with Chlorhexidine Gluconate standard at 0.25% confirmed that the biocidal activity under the above test conditions was found to be equivalent.

The product Hexifoam has shown very rapid biocidal action against the organisms Pseudomonas aeruginosa and Staphylococcus aureus (Our Ref N 17,614). Complete kill of the test organisms was achieved within 1 minute in the in-vitro tests performed to date.

TEST B

A sample of "Hexifoam" was received at the laboratory to be evaluated for its biocidal properties against the organism Staphylococcus aureus.

The product was evaluated in a suspension test in ccordance with the principles outlined in BS. 3286 under the following test conditions.

Product Dilution:	1:2 v/v
Contact Time:	1 minute, 2 minutes, 5 minutes
Organism:	Staphylococcus aureus 4163
Organic Challenge:	10% Sheep Serum
Inoculum Density:	10^6 orgs/ml.,
Product Diluent:	Standard Hard Water - 10% Sheep Serum
Inactivator:	Nutrient Broth No. 2 Lecithin Tween 80
Temperature:	Ambient

Initial count	Final Count per ml *		
	1 Min.	2 Mins.	5 Mins.
2.0×10^6	Less than 10	Less than 10	Less than 10

The Kill Factor achieved in all cases was greater than 2.0×10^5

* Results presented are Geometric Means of duplicate tests.

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TEST C

The product Heixifoam batch 4073 was evaluated for its biocidal activity using a suspension test based on the principles outlined in British Standard BS.3286. The results obtained are as follows:-

Product:	Hexifoam
Test Organism:	C.albicans ATCC 10231
Product Dilution:	1:2 w/v
Diluent:	Distilled water with 10% sheep serum
Organic Challenge:	10% sheep serum
Temperature:	Ambient
Contact Time:	One Minute
Inactivator:	Nitrient Broth No. 2 (Oxoid) with lecithin and tween 80.

Initial Count	Final Count	Kill Factor	% Kill
3.7×10^6	Less than 10	Greater than 3.7 x 105	Greater than 99.99973

Notes

1. Results presented are geometric means of duplicate results.
2. Kill factor is defined as the ratio of initial count versus final count.
3. A kill factor of 10^4 is regarded as significant biocidal activity.

TEST D

The product Hexifoam batch 4073 was evaluated for its biocidal activity using a suspension test based on the principales outlined in British Standard BS.3286. The results obtained are as follows:-

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Product:	Hexifoam
Test Organism:	E.coli NCTC 8196
Product Dilution:	1:2 w/v
Diluent:	Distilled water with 10% Sheep serum
Organic challenge:	10% Sheep serum
Temperature:	Ambient
Contact Time:	One minute
Inactivator:	Nutrient broth No. 2 (Oxoid) with lecithin and tween 80.

Initial Count orgs/ml.	Final Count orgs/ml.	Kill Factor	% Kill
6.7×10^6	Less than 10	Greater than 6.7×10^5	Greater than 99.99986

Notes:

1. Results presented are geometric means of duplicate results.
2. Kill factor is defined as the ratio of initial count versus final count.
3. A kill factor of 10^4 is regarded as significant biocidal activity.

TEST E

The product Hexifoam batch 4073 was evaluated for its biocidal activity using a suspension test based on the principles outlined in British Standard BS.3286. The results obtained are as follows:-

Product:	Hexifoam
Test Organism:	S.typhimurium (clinical isolate)
Product Dilution:	1:2 w/v
Diluent:	Distilled water with 10% sheep serum
Organic Challenge:	10% sheep serum
Temperature:	Ambient
Contact Time:	One Minute
Inactivator:	Nutrient broth No. 2 (Oxoid) with lecithin and tween 80.

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Initial Count Orgs/ml.	Final Count Orgs/ml.	Kill Factor	% Kill
6.7×10^6	Less than 10	Greater than 6.7×10^5	Greater than 99.99986

Notes

1. Results presented are geometric means of duplicate results.
2. Kill factor as defined as the ratio of initial count versus final count.
3. A kill factor of 10^4 is regarded as significant biocidal activity.

TEST F

The product Hexifoam Batch 4073 was evaluated for its biocidal activity using a suspension test based on the principles outlined in British Standard BS.3286. The results obtained are as follows:-

Product:	Hexifoam
Test Organism:	S.aureus (Methicillan Resistant, Clinical Isolate)
Product Dilution:	1:2 w/v
Diluent:	Sterile Distilled Water with 10% Sheep Serum.
Temperature:	Ambient
Contact Time:	One Minute
Inactivator:	Nutrient Broth No.2 (Oxoid) with Lecithin and Tween 80.

Initial Count (Orgs/ml.)	Final Count	Kill Factor	% Kill
4.6×10^6	Less than 10	Greater than 4.6×10^5	Greater than 99.9954%

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Notes:

1. Results presented are geometric means of duplicate results.
2. Kill factor is defined as the ratio of initial count versus final count.
3. A Kill Factor of 10^4 is regarded as significant biocidal activity.

TEST G

The product Hexifoam Batch 4073 was evaluated for its biocidal activity using a suspension test based on the principles outlined in British Standard BS.3286. The results obtained are as follows:-

Product:	Hexifoam
Test Organism:	T.rubrum (clinical isolate)
Product Dilution:	1:2 w/v
Diluent:	Distilled Water with 10% Sheep Serum
Organic Challenge:	10% Sheep Serum
Temperature:	Ambient
Contact Time:	5 minutes
Inactivator:	Nutrient Broth No.2 (Oxoid) with lecithin and Tween 80

Initial Count Orgs/ml.	Final Count Orgs/ml.	Kill Factor	% Kill
1.0×10^7	Less than 10	Greater than 1.0×10^6	Greater than 99.9999

Notes

1. Results presented are geometric means of duplicate results.
2. Kill factor is defined as the ratio of initial count versus final count.

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TEST H

Hexifoam was evaluated in our laboratory in a short, preliminary in-vivo trial using various dosages and exposure times against Pseudomonas aeruginosa NCTC 6749.

Experimental Design

Two volunteers from our laboratory were used. For the duration of the experiment the hands of the personnel were allowed to be washed only with traditional bar soap. No chlorhexidine based products such as our standard laboratory scrub were used to ensure there was no build up of chlorhexidine on the skin. The time interval between Hexifoam trials was at least three days.

Fresh 24 hour suspension cultures of P.aeruginosa NCTC 6749 were utilised for each trial. Cultures were grown in Wright and Mundy broth (Difco) for 24 hours at $37^{o}C$.

One ml. of P.aeruginosa representing at least 1×10^{9} cells was applied to the palm of one hand. This was then carefully rubbed over the surface of both hands. No culture was allowed to be dropped from the hands during this operation. If so the trial was declared void at that time, the person washed their hands and the inoculation was repeated after a break of at least two hours. The culture was allowed to dry completely on the hands before application of Hexifoam.

Hexifoam was weighed on tc a plastic square and then applied to the hands. This procedure ensured accurate dosage by weight. The Hexifoam was rubbed over the entire surface of the hands. Exposure time was monitored with a stop watch. At the end of the allocated exposure time the hands were placed into 500 ml. of inactivator solution comprising 3% tween 80, 2% lecithin. For one minute the hands were scrubbed in the inactivator solution to release any surviving P.aeruginosa into the liquid.

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Trial Description	Weight of Hexifoam Used (g)	Exposure Time (sec)
Recovery Control	0	0
Test 1	1	30
Test 2	2	30
Test 3	2	60

Results

Recovery Control

Culture Count onto Hands Total Cells	Control Recovery Total Cells		% Recovery		Geometric Mean % Recov-
	Volunteer		Volunteer		
	1	2	1	2	
2.8×10^9	5.5×10^6	21.0×10^6	0.196	0.750	0.384

0.384% is used to calculate the expected recovery in all Hexifoam trials. This adjusts for culture variation and is needed to calculate reductions achieved.

Hexifoam Trials

Trial Description	Culture Count onto Hands Total Cells (y)	Recovery Total Cells Volunteer	
		1	2
1 g 30 Sec	3.1×10^9	1.3×10^6	3.2×10^6
2 g 30 Sec	2.6×10^9	5.0×10^5	5.5×10^5
2 g 60 Sec	4.3×10^9	2.55×10^4	11.5×10^4

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Trial Description	Geometric mean Recovery	Calculated Recovery 0.384% x y	Mean Log Reduction	Kill
1 g 30 Sec	2.03×10^6	11.9×10^6	0.768	82.95
2 g 30 Sec	5.24×10^5	10.0×10^6	1.281	94.76
2 g 60 Sec	5.4×10^4	16.5×10^6	2.485	99.67

The foamable compositions within the present invention improve over prior chlorhexidine products commercially available as follows:-

(1) As a pressurised aerosol the pack cannot become internally contaminated.

(2) The aerosol cannot spill and therefore represents no fire hazard.

(3) The foam, as dispensed, is very hard to ignite and will not readily burn as does a spray, presenting a much reduced hazard.

(4) The foam is easily handled and does not allow any waste due to overspray.

(5) The foam as developed is of a fast breaking variety. When applied to the skin it is a stable lump, but body heat or friction cause it to melt and spread onto the skin in a unique, controllable, and fast dispersing manner.

(6) The shelf life of the aerosol is good and with some formulation is probably in excess of five years almost irrespective of the storage environment.

(7) Since a ball of foam can be held in one hand the pack only needs to be touched once and the treated hands never need to come into contact with it.

Quite unexpectedly, having regard to the prior research carried out the stated combination has in testing exceed performance expectation. Further, as disclosed initial microbiological tests have shown the compositions retain the full broad specrum of activity of chlorhexidine

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and to be surprisingly fast acting, killing 99% plus of M.R.S.A. in less than sixty seconds. This result is clearly superior to conventional chlorhexidine compositions.

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THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. A biocidal composition comprising:
   (a) an alcoholic chlorhexidine solution
   (b) from .1 to 20% w/w of a quick breaking foaming agent
   (c) from 3 to 30% w/w of an aerosol propellant and optionally
   (d) a corrosion inhibitor

2. The composition of claim 1 wherein the chlorhexidine solution is present in amounts from .1 to 10% w/w.

3. The composition of claim 1 wherein the chlorexidine solution is in the form of a gluconate, diacetate hydro chloride or mixtures thereof.

4. The composition of claim 1 wherein the foaming agent comprises an aliphatic alcohol, water, a fatty alcohol and a surface active agent.

5. The composition of claim 4 wherein the aliphatic alcohol is present in amounts of from 40 - 90% ww, water is present in amounts from 10 - 40% w/w, the fatty alcohol is present in amounts of from 0.5 - 10% w/w and the ethoxylated sorbitan ester is present in amounts of from 0.1 - 15% w/w.

6. The composition of claim 4 wherein the aliphatic alcohol is selected from the group including methanol, ethanol, isopropanol and butanol and mixtures thereof.

7. The composition of claim 4 wherein the fatty alcohol is selected from the group including cetyl alcohol, stearyl alcohol, lauryl alcohol, myristyl alcohol, palmityl alcohol and mixtures thereof.

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8. The composition of claim 4 wherein the surface active agent is selected from the group including ethoxylated sorbitan stearate, palmitate, oleate, nonyl phenol ethoxylates, fatty alcohol ethoxylates and mixtures thereof.

9. The composition of claim 1 wherein the propellant is selected from the group including propane, butane, dichlorodifluoro methane, dichloro tetra fluoro ethane, octafluoro cyclo butane and mixtures thereof.

10. The composition of claim 1 wherein the corrosion inhibitor is present in amounts of from .1 - 15% wt.

11. The composition of claim 1 wherein the corrosion inhibitor is an organic acid salt.

12. The composition of claim 11 wherein the organic acid salt is selected from the group including sorbic acid benzoic acid, mixtures thereof and soluble forms thereof.

13. The composition of claim 12 wherein the organic acid is present in an amount of from 0.1 to 3% w/w.

14. The composition of claim 1 further including an emollient.

15. The composition of claim 13 wherein the emolient is selected from the group including lanolin, polyols selected from the group including glycerol, propylene glycol, sorbitol and low molecular weight polymers thereof, vinyl alcohol and polyvinyl pyrollidone.

16. A biocidal composition comprising:

(a) 0.1 to 10% w/w of chlorhexidine

(b) 0.1 to 20% w/w of a quick breaking foam

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comprising

(1) 40 to 90% ww of an aliphatic alcohol

(2) 0.5 to 10% ww of a fatty alcohol

(3) 10 to 40% ww water

and

(4) 0.1 to 15% ww of an ethoxylated sorbitan ester

(c) 3 to 30% w/w of an aerosol propellant

and optionally

(d) 0.1 - 15% corrosion inhibitor.

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INTERNATIONAL SEARCH REPORT

International Application No PCT/AU84/00215

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all) [3]

According to International Patent Classification (IPC) or to both National Classification and IPC

INT. CL[3] A61K 31/155

II. FIELDS SEARCHED

Minimum Documentation Searched [4]

Classification System	Classification Symbols
IPC	A61K 31/15, A61K 27/00, A01n 47/44
US CL	424/45, 424/47

Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched [5]

AU : AUSTRALIAN CLASSIFICATION 87.16-0

III. DOCUMENTS CONSIDERED TO BE RELEVANT [14]

Category *	Citation of Document, [16] with indication, where appropriate, of the relevant passages [17]	Relevant to Claim No. [18]
A	AU, B, 51132/73 (472449)(UNILEVER LIMITED) 18 July 1974 (18.07.74) See Page 8	
A	AU, A, 10754/70 (MEDILINE AG) 12 August 1971 (12.08.71) See Pages 12-14	
A	AU, A, 65156/69 (MEDILINE AG) 17 June 1971 (17.06.71) See Page 12	

* Special categories of cited documents: [15]

"A" document defining the general state of the art which is not considered to be of particular relevance

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IV. CERTIFICATION

Date of the Actual Completion of the International Search [2]	Date of Mailing of this International Search Report [2]
25 January 1985 (25.01.85)	30.01.85 30 JANUARY 1985
International Searching Authority [1]	**Signature of Authorized Officer [20]**
Australian Patent Office	R. DALBON

Form PCT/ISA/210 (second sheet) (October 1981)

ANNEX TO THE INTERNATIONAL SEARCH REPORT ON
INTERNATIONAL APPLICATION NO. PCT/AU **84/00215**

This Annex lists the known "A" publication level patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent Document Cited in Search Report	Patent Family Members					
AU 65156/69	BR	6915170	CH	544548	DE	1964539
	ES	374808	FR	2026873	GB	1296360
	NL	6919223				
AU 10754/70	BE	745339	DE	2004610	ES	376140
	FR	2033831	GB	1304682		
AU 51132/73	AR	193183	BE	794067	BR	7300449
	CA	1003333	CH	572741	DE	2301829
	FR	2168463	GB	1409533	IN	138618
	IT	1009022	JP	48080744	LU	66835
	NL	7300718	US	3949066	ZA	730352

END OF ANNEX